Identifying Brain Regions Supporting Amygdalar Functionality: A Complex Anatomical Network Perspective

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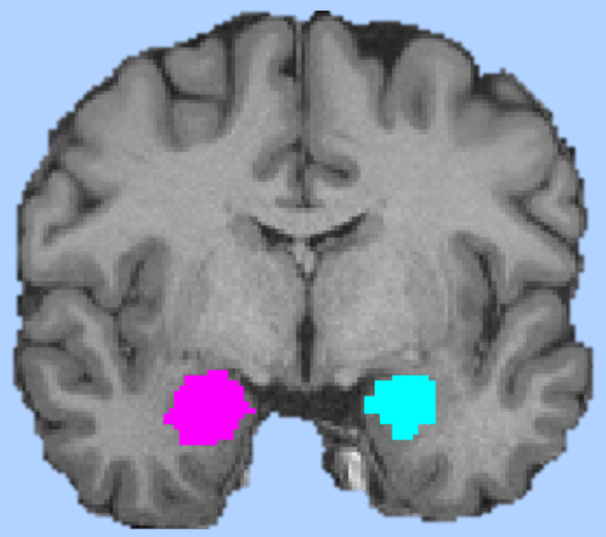
Introduction

Amygdala importance

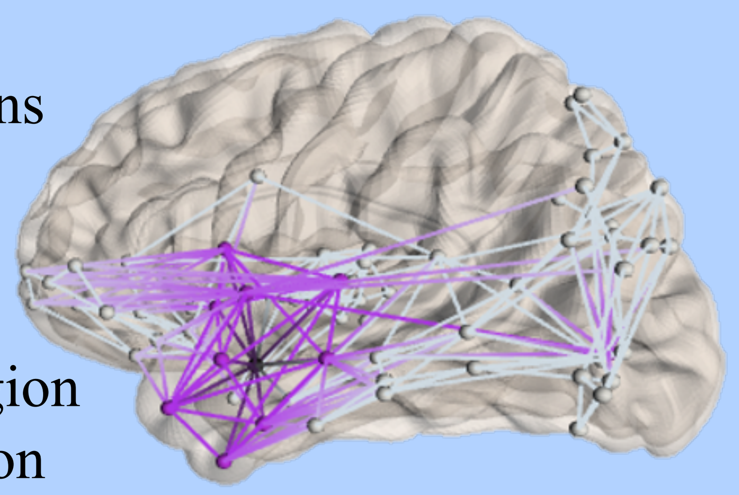
- •Critical to motivational & emotional processes



- •Moderating perception & attention
- •Fear conditioning
- •Psychiatric disorders (LeDoux, 2007)

- •Past amygdala function research focus:
  - •Activation within amygdala
  - •Connection with single regions

Brain networks



- •Model the patterns of connections between brain regions
- •Node = brain region
- •Edge = connection between 2 nodes (brain regions)

Graph theory methods

- •Index emergent properties of brain networks
- •Phenomena of interest (e.g., emotion) also emergent property of the brain
- •Thus, network metrics may come closer to capturing emergent phenomena of the brain

Gap in the literature

- •Amygdala does not function alone but relies on a complex network of brain regions
- •How do different aspects of amygdalar influence emerge from structural connections within the global brain network?

Present study

- •Employ 'virtual lesioning' method to structural networks to identify sets of brain regions needed to support several effective amygdalar interactions with network

Methods

Participants & data acquisition

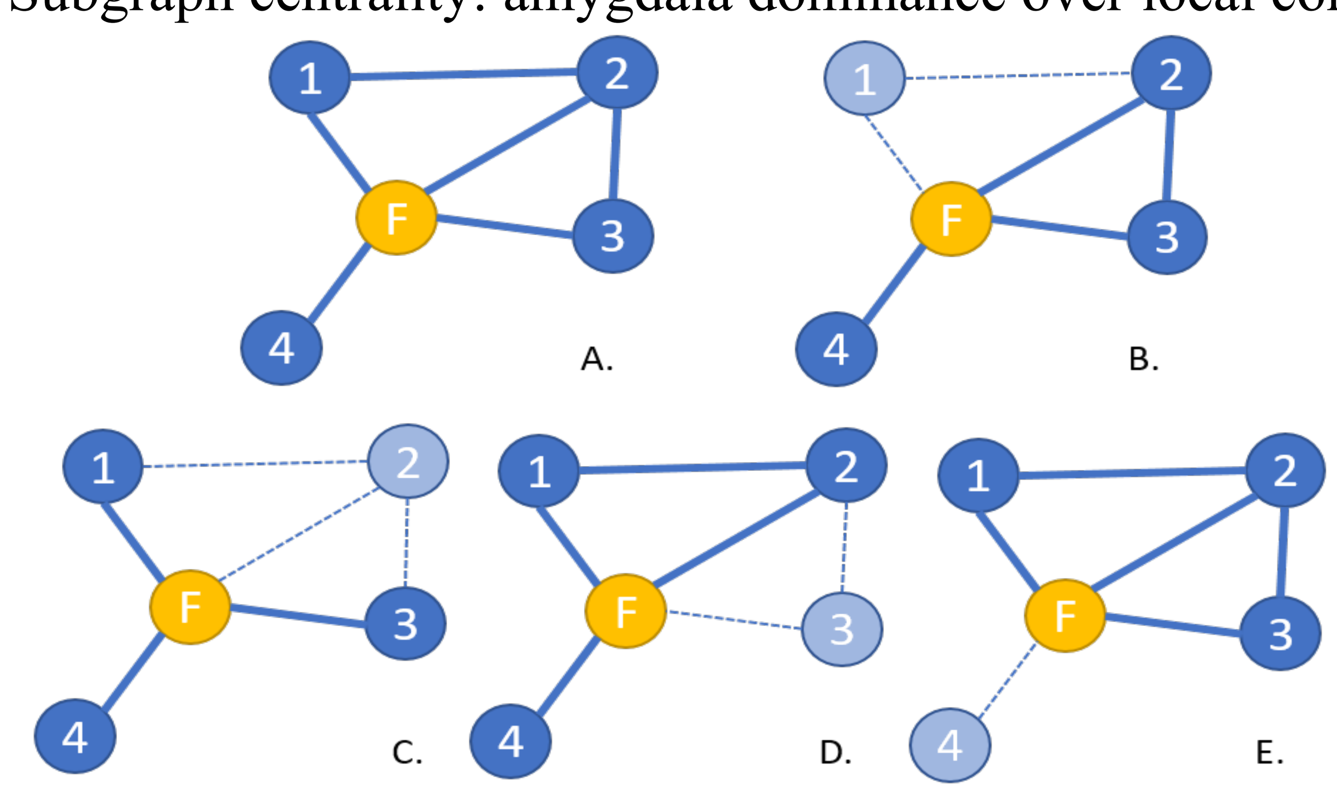
- •N=1052 healthy adults (M age=28.75, F=571); from the Human Connectome Project (HCP) (Van Essen et al., 2013)
- •Structural and diffusion-weighted imaging (DWI) data

Data analysis

1. Use FSL to calculate white matter networks from diffusion MRI data (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012)
2. For each participant's network, perform virtual lesion method separately for each centrality metric
3. Paired F-tests of difference (reduced - full network) in centrality metrics for each satellite node across participants (Graph Theory GLM Toolbox)
   1. Test whether difference in a given metric different from that of each other metric
   2. False discovery rate (FDR) to correct for multiple comparisons across nodes

Centrality

- •Indexes importance and influence for a specific node in the network
- •Betweenness centrality: control over information flow; extent to which a region is a bottleneck for information flow
- •Node communicability: clarity of amygdala communication with network nodes; ability to transmit information without interference
- •Subgraph centrality: amygdala dominance over local communication



Virtual lesion method

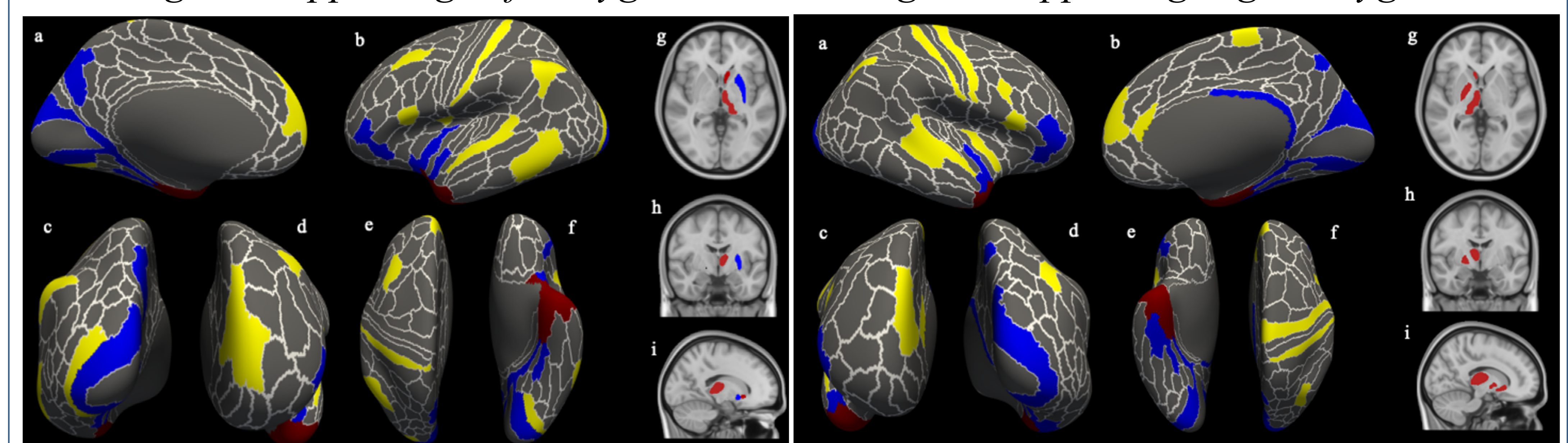
- •Centrality is first calculated for the full network (A)
- •Centrality recalculated after removing nodes iteratively (B-E)
- •Change in centrality of node of interest (F) calculated for each node
- •Subtract centrality of full network (A) from each reduced network (B-E)

Results

•Betweenness, communicability, subgraph centrality each associated with separable sets of regions, some of which map onto previously identified sub-circuits

- •Anterior (*communicability*) and Posterior (*betweenness*) Temporal Systems for memory-guided behavior (Ranganath and Ritchey, 2012)
- •Conceptualization and labeling of core affect (*subgraph*) (Lindquist et al., 2012)

Regions Supporting Left Amygdala *Regions Supporting Right Amygdala*



Regions supporting amygdala centrality are colored: current-flow betweenness centrality, blue, node communicability, red, subgraph centrality, yellow. (A-F) cortical regions, (G-I) subcortical regions. Left: (A) medial, (B) lateral, (C) posterior, (D) anterior, (E) superior, (F) inferior. Right: (A) lateral, (B) medial, (C) anterior, (D) posterior, (E) inferior, (F) superior. (G) axial, (H) coronal, (I) sagittal.

Discussion

Goal

- •Leverage unique positions each brain region occupies in the network to determine their contribution to supporting amygdala influence over the network
- •Gain insights into a normative framework supporting amygdala function

Highlights

- •We identified nodes crucial to supporting amygdala function
  - •Related to memory, emotion, and sensory processing
- •Different emergent aspects of amygdalar communication (i.e., graph properties) were associated with separable sets of regions depending on specific function

Future directions

- •Examine manner in which pathological amygdala processes arise by identifying deviations from the defined normative framework

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